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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,464	02/17/2004	Srinivasa Madhyastha	14233.15USU1	1780

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/781,464	MADHYASTHA, SRINIVASA	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *15-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 32-34* is/are rejected.

7)☒ Claim(s) *12-14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 February 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/21/04;8/25/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-14 and 32-34 in the response filed February 1, 2005, and further election of a composition of a iron-sequestering glycoprotein, a cationic polypeptide and a chelating agent (part a) in claim 1, ovotransferrin from claim 8 and protamine sulfate from claim 9 in the supplemental response filed April 4, 2005 are acknowledged. The traversal is on the ground(s) that sufficient reasons and examples are not provided for restriction requirement, and it would not be unduly burdensome to search the claims of Group II since the search of the composition of Group I would likely encompass the method of treating a surface with the compositions of Group I. Applicants further indicate it would not be unduly burdensome to search part (b) and (c) of claim 1, and the compositions including various iron-sequestering glycoproteins (claim 8) and cationic polypeptides (claim 9) since the search of the composition of part (a) would likely encompass parts (b) and (c), and the compositions of claims 8 and 9. The argument is not found persuasive regarding searching Group II because coexamination of Group II claims would require search of subjects unnecessary for the examination of Group I, e.g., medical devices. Furthermore, the claimed composition is searched in light of its components and not its intend use or functional characteristics. Therefore, coexamination of Group II would require a serious additional burden of search.

The restriction groups have acquired a separate status in the art as a separate subject for inventive effect and require independent searches. The search for each of the invention is not coextensive particularly with regard to the literature search. A reference which would anticipate

the invention of one group would not necessarily anticipate or make obvious any of the other group. Moreover, as to the question of burden of search, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues also exist.

Regarding searching and examining parts (b) and (c) of claim 1 and the compositions including various iron-sequestering glycoproteins (claim 8) and cationic polypeptides (claim 9), the argument is persuasive. Thus, claims 1-14 and 32-34 including various compositions are examined, and claims 15-31 are non-elected invention and withdrawn from consideration.

The requirement is still deemed proper and is therefore made FINAL.

Priority

2. Applicant's claim for foreign priority based on a Canadian patent application filed December 4, 2003 (see Oath and continuation data at page 1 of the specification), however, the application number has not been provided. Furthermore, that applicant has not filed a certified copy of the foreign application as required by 35 U.S.C. 119(b). Therefore, the claimed foreign priority is not perfected.

Informalities

The disclosure is objected to because of the following informalities:

3. In the continuation data at page 1, paragraph [0002] of the specification, the application number for a Canadian patent application filed December 4, 2003 is missing. Appropriate correction is required.

4. The drawings are objected to for containing figure legends. The figure legends in the drawings are unacceptable and belong to the brief description of drawing in the specification. Figs. 1-12 are also objected to because of the size of the drawings, it appears very crowded by making three drawings on one sheet of paper.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-11 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition of ovotransferrin, protamine sulfate and EDTA, of ovotransferrin and protamine sulfate, or of ovotransferrin and EDTA, which inhibits bacterial biofilm on devices; or a composition of lactoferrin and lysozyme, or of ovotransferrin and lysozyme as indicated in the prior art, does not reasonably provide enablement for a composition for inhibiting bacterial biofilm on devices, the composition comprising an iron-sequestering glycoprotein, a cationic polypeptide, and a chelating agent; or an iron-sequestering glycoprotein and a cationic polypeptide; or an iron-sequestering glycoprotein and a chelating agent, wherein the iron-sequestering glycoprotein, the cationic polypeptide or the chelating agent in the composition is not defined. The specification does not enable persons skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-11 and 32-34 encompass a composition for inhibiting bacterial biofilm on devices, the composition comprising an iron-sequestering glycoprotein, a cationic polypeptide,

and a chelating agent; or an iron-sequestering glycoprotein and a cationic polypeptide; or an iron-sequestering glycoprotein and a chelating agent. The specification, however, only discloses cursory conclusions (sees pages 6-8), without data to support the findings, which state that the instant invention provides a composition comprising a small amount of an iron-sequestering glycoprotein and a sparing amount of a cationic polypeptide; a composition comprising a small amount of an iron-sequestering glycoprotein and a sparing amount of a chelating agent; or a composition comprising a small amount of an iron-sequestering glycoprotein, a sparing amount of an iron-sequestering glycoprotein and a small amount of a chelating agent, where the combination is sufficient to form a synergistic antimicrobial composition. There are no indicia that the present application enables the full scope in view of a composition of an iron-sequestering glycoprotein, a cationic polypeptide, and/or a chelating agent as discussed in the stated rejection. The present application does not provide sufficient teaching/guidance as to how the full scope of the claims is encompassed. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the iron-sequestering glycoprotein, the cationic polypeptide, and/or the chelating agent in the

composition, and the synergistic antimicrobial effect of the composition, where are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

Examples 1-5 indicate effects of ovotransferrin (OT), protamine sulfate (PS) and EDTA alone and in combinations on biofilm formation in catheter-associated bacteria (Example 1); effects of synergistic composition on biofilm formation by catheter-associated bacteria in urinary catheter (Example 2); effect of synergistic composition on the viable cell counts of catheter-associated bacteria (Example 3); effect of coating urinary catheter with tridodecyl methyl ammonium chloride (TDMAC) plus synergistic antimicrobial composition on the growth of catheter-associated bacteria (Example 4); and effect of coating urinary catheter with polyvinylpyrrolidone (PVP) hydrogel plus synergistic antimicrobial composition on the growth of catheter-associated bacteria (Example 5). However, there are no working examples indicating the claimed composition in association with numerous variants.

(3). The state of the prior art and relative skill of those in the art:

The prior art (e.g., Leitch *et al.*, Current Eye Research 19, 12-9 (July 1999)) disclose the use of a composition of lactoferrin and lysozyme in the treatment of *Staphylococus epidermidis* biofilm infection. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the identification of various iron-sequestering glycoproteins, cationic polypeptides, and chelating agents used in the synergistic antimicrobial composition to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The specification describes the synergistic antimicrobial composition of ovotransferrin (OT), protamine sulfate (PS) and/or EDTA against bacterial biofilm formation, however, the specification has not identified various iron-sequestering glycoproteins, cationic polypeptides, and chelating agents used in the synergistic antimicrobial composition, nor has demonstrated their effects on inhibiting bacterial biofilm. The invention is highly unpredictable regarding the components of the synergistic antimicrobial composition, and the inhibitory effect of the composition.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a composition for inhibiting bacterial biofilm on devices, the composition comprising an iron-sequestering glycoprotein, a cationic polypeptide, and a chelating agent; or an iron-sequestering glycoprotein and a cationic polypeptide; or an iron-sequestering glycoprotein and a chelating agent. The specification only demonstrates the synergistic antimicrobial composition of ovotransferrin (OT), protamine sulfate (PS) and/or EDTA against bacterial biofilm formation (Examples 1-5), there are no examples indicating various iron-sequestering glycoproteins, cationic polypeptides, and chelating agents used in the synergistic antimicrobial composition. The specification has not identified various synergistic antimicrobial compositions, nor has demonstrated the inhibitory effects of these compositions on bacterial biofilm formation. Since the specification does not provide specific guidance on the identification of various iron-sequestering glycoproteins, cationic polypeptides, and chelating agents used in the synergistic antimicrobial composition, it is necessary to have additional

guidance and to carry out further experimentation to identify the components of he composition and to assess the inhibitory effect on bacterial biofilm formation.

(6). Nature of the Invention

The scope of the claims includes various synergistic antimicrobial compositions, but the specification does not provide sufficient teachings on the identification of various components in the composition and their effects on bacterial biofilm formation. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed composition associated with variants, and the guidance/the teaching in the specification is limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the inhibitory effects of synergistic antimicrobial compositions on bacterial biofilm formation.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is indefinite because of the use of the term "EDTA, EGTA.....NTA". The term renders the claim indefinite, it is not clear what the term represents. A fully spelled word should be indicated for each chemical abbreviation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 2, 5, 7-9, 11 and 32-34 are rejected under 35 U.S.C. 102(b) as anticipated by Leitch *et al.* (Current Eye Research 19, 12-9 (July 1999)).

Leitch *et al.* disclose the use of a composition of lactoferrin and vancomycin or lysozyme in the treatment of *Staphylococus epidermidis* biofilm infection (abstract). The viability of cells from the intact biofilm was determined, when lenses coated with S. epidermidis biofilm were incubated overnight at 37 °C in TSB (tryptone soya broth) containing lysozyme (2, 4, 8, 16 mg/ml) or vancomycin in the presence or absence of lactoferrin (1024 mg/L; page 13, right column, third paragraph; claims 2, 11), where the combination of lysozyme and lactoferrin reduced the number of viable biofilm and biofilm-released cells compared to the growth of cells treated with lysozyme alone (Fig. 3; page 16, left column, paragraph 3; claims 1, 5, 7-9 and 32-34).

8. Claims 1-3, 6, 8, 9, 11 and 32-33 are rejected under 35 U.S.C. 102(b) as anticipated by Ellison *et al.* (J. Clin. Invest. 88, 1080-1091 (1991)).

Ellison *et al.* disclose a combination of lactoferrin and lysozyme has bactericidal effect, where lactoferrin enhanced the activity of lysozyme (Fig. 2; claim 1). For example, various concentrations of lactoferrin (0.5, 1, 2 or 4 mg/ml; claims 2, 8) and lysozyme (0.0063, 0.0125, 0.025 or 0.05 mg/ml; claims 3, 9, 11) were tested against E. coli 5448 (Fig. 3; page 1082, right

column), the synergistic activity of the two proteins was found to be dependent on either lactoferrin (Fig. 3A) or lysozyme (Fig, 3 B). Since a composition, which contains the same effective amounts of lactoferrin and lysozyme as the claimed invention, is used for inhibiting E. coli, it would be expected the composition is effective against biofilms of E. coli, which meet the criteria of claims 6, 32 and 33. The term "for inhibiting bacterial biofilm on devices" is an intended use, which does not give weight on a composition claim.

9. Claim 1 is rejected under 35 U.S.C. 102(b) as anticipated by Johnson (Egg Uses and Processing Technologies (1994), 177-191, edited by J. S. Sim & S. Nakai).

Johnson discloses activity of lysozyme against yeast was potentiated by lysolecitin or polylysine (Table 15.2), where a combination of lysozyme and conalbumin (ovotransferrin) is also tested against various yeasts (pages 181-182, claim 1). The term "for inhibiting bacterial biofilm on devices" is an intended use, which does not give weight on a composition claim.

Claim Objections

10. Claims 12-14 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

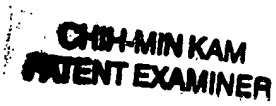
11. Claims 1-11 and 32-34 are rejected; and claims 12-14 are objected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner



CMK
June 7, 2005